UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/590,986	08/29/2006	Michio Yamamura	0020-5507PUS1	2444

2292 7590 06/30/2008

BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER	
CRANE, LAWRENCE E	

ART UNIT	PAPER NUMBER
1623	

NOTIFICATION DATE	DELIVERY MODE
06/30/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/590,986	YAMAMURA ET AL.	
	Examiner	Art Unit	
	Lawrence E. Crane	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *March 10, 2008 (amdt and declaration)*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-6 and 9-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-6 and 9-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 August 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The Abstract of the Disclosure is objected to because is does not meet the requirement of the MPEP for US application. Correction is required. See MPEP 608.01(b).

Applicant is reminded of the proper content of an Abstract of the Disclosure.

In chemical patent abstracts, compounds or compositions, the general nature of the compound or composition should be given as well as its use, e.g., "The compounds are of the class of alkyl benzene sulfonyl ureas, useful as oral anti-diabetics." Exemplification of a species could be illustrative of members of the class. For processes, the type reaction, reagents and process conditions should be stated, generally illustrated by a single example unless variations are necessary. Complete revision of the content of the abstract is required on a separate sheet.

Applicant is respectfully requested to amend the abstract because the present Abstract is not grammatically complete; the abstract is at present not a complete sentence. Following the term "comprising D-ribose" at line 1, examiner respectfully suggests the simple insertion of the term -- is disclosed -- would correct this oversight.

Claims **3 and 7-8** have been cancelled, claims **1, 2, 4-6 and 9** have been amended, the disclosure and the Abstract have been amended, and new claims **10-13** have been added as per the amendment filed March 10, 2008. No additional or supplemental Information Disclosure Statements (IDSs) have been filed as of the date of this Office action. A declaration also filed March 10, 2008, apparently under 37 C.F.R. §1.132, and signed by Mssr. Asahi has also been received, made of record and considered during the preparation of this Office action. The **Cryan et al.** reference, a copy of which has been kindly provided by applicant, has been made of record on an updated PTO-892 attached hereto and has been reviewed during the preparation of this Office action.

Claims **1, 2, 4-6 and 9-13** remain in the case.

The disclosure is objected to because of the following informalities:

At page 8 of the disclosure at lines 11 and 12, the terms "Vitamin As, Vitamin Bs, Vitamin Cs, Vitamin Ds, Vitamin Es" includes numerous errors of fact; e.g. there is only one -- vitamin C --. Examiner suggests that the noted term may be amended to read -- vitamin A, B

vitamins, vitamin C, vitamin D, vitamin E --. In addition at line 12, the term "nicotine acid" appears to be a technical misspelling of the term -- nicotinic acid --. In addition at line 13, the term "pantethine" appears to be a misspelling of the term -- pantothenic acid --(?), a compound also known to be a B vitamin (check medical dictionaries and/or biochemistry texts).

Appropriate correction is required.

Claim **1** is objected to because of the following informalities:

In claim **1** at line 6, the term "drop in operation efficiency" is grammatically incorrect. Did applicant intend this term to read -- drop in operational efficiency -- ? Also at line 8, the term "not accompanied by alcoholism" appears to include a wrong word. Did applicant intend this term to read -- not caused by alcoholism -- ?

Appropriate correction is required.

Note to applicant: In the personal interview with Attorney Murphy and applicant's representative Ms. Sato, examiner raised the issue of the the D-ribose or D-ribose equivalent content (e.g. ribosylated vitamins including B_{12} and L, etc.) of the animal feed provided to the test subjects. Applicant has misunderstood this question and has disclosed that supplemental D-ribose was not added to the feed. Examiner renews the question and respectfully requests a complete listing of all ingredients in the feed in order to establish a baseline D-ribose plus D-ribose equivalent intake.

Claims **1, 2, 4-6 and 9-13** are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabled for administration of ribose or ribose plus potassium magnesium aspartate to improve mammalian physical performance when under stress as well as memory performance, does not reasonably provide enablement for the treatment of the vast array of other disease conditions encompassed in claims **1, 2 and 9-12** by the generic term "depressive symptoms" that is further elaborated in claim **1** by the terms "indefinite complaint," "decline in thinking power," "impaired sight," "mental overstrain," "mental disorder," "feeling of malaise," etc., etc. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The fundamental issue here is whether practicing the full scope of the instant invention is possible without undue experimentation. As provided for in *In re Wands* (858 F.2d 731, 737; 8 USPQ 2d 1400, 1404 (Fed Cir. 1988) the minimum factors to be considered in determination of whether a conclusion of "undue experimentation" is appropriate are as follows:

A. The breadth of the claims: The claims are directed to the treatment directed to "improving depressive symptoms which comprises," a term that, courtesy of the presence of the term of art "comprises," is not limited to the specific symptoms listed and therefore has a breadth that greatly exceeds the scope of the enabled embodiments. The breadth of the claims is clearly excessive in view of the limited number of specific exemplifications.

B. The nature of the invention: This subject is dealt with by the previous paragraph.

C. The state of the prior art: The administration of ribose to treat various conditions in mammals or to promote improvements in the physical condition/performance of mammals is well known in the art as clearly and repeatedly established by the prior art of record.

D. The level of one of ordinary skill: Based on the extensive disclosures found in the prior art, one of ordinary skill would be expected to the size of effective dosages of ribose and to know how to administer an effective dose of ribose to a mammalian host.

E. The level of predictability in the art: The predictability in this are is a function of what physiological results is desired and what is known about obtaining this kind of result in the prior art. At present the prior art of record has very little disclosure of the effect of ribose in mental functions per se, but does suggest that ribose administration does improve ATP generation and may be administered in a strength increasing regimen.

F. The amount of direction provided by the applicants including working examples: The instant disclosure include 6 working examples and one comparative example wherein lower mammals directed to measuring the effects of ribose in various test regimens wherein lower mammals are stressed by the requirement for physical exertion (e.g. swimming when weighted) and wherein humans are tested for memory acuity with and without ribose supplementation. However, there is no data showing effective treatment of human hosts established to be suffering from depressive symptoms.

G. The existence of working examples: This subject is dealt with by the previous paragraph.

H. The quantity of experimentation needed to make or use the invention based on the content of the disclosure is deemed to be excessive because the terminology provided in the claims to define the conditions to be treated far exceeds a reasonable interpretation of what conditions are actually effective treated and therefore enabled by the test regimens disclosed.

Applicant's arguments filed March 10, 2008 have been fully considered but they are not persuasive.

Applicant argues that the instant claims are enabled on the basis that the theory of the "modified rat forced swimming test" as described in the **Cryan et al.** reference (PTO-892 ref. **T**) in combination with the declaration of **Asahi** provides an adequate basis therefore; i.e. that the theory of the **Cryan et al.** reference is the only, or at least the best, basis for interpretation of the test data disclosed herein and by the **Asahi** declaration. Examiner respectfully disagrees, and notes the first paragraph of the **Palazzi et al. '311** reference (WO92/15311; PTO-1449 ref. **A2**) wherein said document discloses that the administration of D-ribose alone or D-ribose in combination with a magnesium salt causes and increase in ATP production. In view of the notoriously well known in the art fact that ATP is the energy source of mammalian cells, examiner considers that the **Palazzi '311** reference's disclosure provides a convincing alternative explanation for the effect observed by applicant; i.e. that D-ribose or D-ribose plus a magnesium salt causes mammalian cells to increase ATP production and therefore causes an improvement in mammalian mood as reflected by an increased ability to execute mental and physical tasks (e.g. overcoming "sluggishness," etc. etc. As noted in The Merck Manual at Chapter 2, pages 27 and 29 ("Symptoms and Signs" - see column 2 of both pages), the symptoms of two varieties of malnutrition include lack of energy ("patient feels week"), "petulance," "apathy," and "irritability." Applicant is respectfully requested to provide any additional showing that may distinguish between the treatment of "depressive symptoms" and the treatment of malnutrition, because the symptomologies of these two conditions are clearly overlapping.

And lastly, examiner notes the Asahi declaration and finds that the data submitted therein is relevant but does not add very much to the knowledge disclosed in the instant application.

At least one of the instant cited patents **(Cyr et al. '480**; PTO-892 ref. **F**; US **6,534,480)** discloses at column 3, lines 37-46, that D-glucose administration is less effective in enhancing energy (ATP) output at the cellular level than D-ribose administration because of the intervening enzymatic pathways that must be traversed to obtain the necessary phosphorylated D-ribose intermediate from D-glucose *in vivo*. The data obtained by Asahi merely confirms the above noted disclosure in **Cyr et al. '480**.

Claims **10 and 13** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim **10** at line 3, the term "and magnesium" is technically incorrect because the administration of magnesium metal is implied thereby. Did applicant intend the noted term to read
-- and a pharmaceutically acceptable magnesium salt --?

Applicant's arguments with respect to claims **1-9** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's amendments.

In claim **10** at line 4, the term "selected from" is a Markush preamble but at line 6, the term "or" is present near the end of the line. Examiner respectfully suggests that applicant substitute the term
-- and -- for the term "or" in order to make the Markush group properly complete, or to reformulate the claim so that the Markush preamble may be eliminated.

Applicant's arguments with respect to claims **1-9** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's amendments.

In claim **13** the term "subject is also administered magnesium" is both technically erroneous and lacks proper antecedent basis in claim **12**. Examiner respectfully suggests that the noted term may be amended to read -- method further comprises administration of a pharmaceutically acceptable magnesium salt --.

Applicant's arguments with respect to claims **1-9** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's amendments.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

"A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent."

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States."

(e) the invention was described in

(1) an application for patent described under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application filed under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a)."

(f) he did not himself invent the subject matter sought to be patented."

Claims **1, 2, 4 and 9-13** are rejected under 35 U.S.C. §102(**a**) and (**e**)) as being anticipated by **Vazquez et al. '027** (PTO-892 ref. **E**, US **6,525,027**).

Applicant is referred to column 6 of the instant reference wherein the administration of compositions comprising ribose and optionally further comprising L-carnitine and a magnesium compound to a human host to improve stamina is disclosed in claims ***1-6***. These claims anticipate the instant claimed subject matter because the administration of D-ribose or D-ribose with the additional noted substances, is disclosed to cause an increase in stamina, a finding that overlaps with the effective treatment of the symptoms "general fatigue,"."sluggishness," and "drop in operation[al] efficiency." listed in claims **1 and 2** as included within the scope of "depressive symptoms."

Applicant's arguments filed March 10, 2008 have been fully considered but they are not persuasive.

Applicant alleges that the claims as now in the case are not anticipated by the instant noted reference. Examiner respectfully disagrees, noting that the disclosure of **Vasquez et al. '027** includes active ingredients that meets the limitations of the instant noted claims and has effects which overlap with the symptoms applicant alleges are effectively treated by the administration of D-ribose and optionally with the administration of a magnesium compound and or the amino acid L-carnitine.

Therefore, even though the **'027** reference does not allege the treatment of "depressive symptoms," the instant claims are anticipated by the claims of the **'027** reference, particularly the **'027** reference at claims ***1 and 6***, because the effective treatments of the symptoms disclosed herein overlap with the observed effects of D-ribose administration found in the **Vasquez et al. '027** reference. In effect the included term "depressive" in the instant preambles fails to distinguish the instant claims from the prior art.

The following is a quotation of 35 U.S.C. §103(**a**) which forms the basis for all obviousness rejections set forth in this Office action:

> "A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made."

Claims **1, 2, 4-6 and 9-13** are rejected under 35 U.S.C. §103(**a**) as being unpatentable over **Vazquez et al. '027** (PTO-892 ref. **E**) in view of **Palazzi et al. '311** (PTO-1449 ref. **A2**) and further in view of the **Hayashida et al.** reference (PTO-892 ref. **U**) and the Aashi declarations admissions concerning the contents thereof.

The instant claims are directed to compositions containing ribose or a mixture of ribose, carnitine and a magnesium salt of aspartic acid or only a composition containing ribose as the active ingredient.

Vazquez et al. '027 discloses at column 1, lines 48-55, the paragraph bridging columns 1 and 2 ending at lines 1-2 of column 2, and at column 2 at lines 46-50 compositions wherein

ribose alone or ribose in combination with other ingredients including L-carnitine and a magnesium compound have been disclosed. The reference also claims the administration of the above-defined compositions to improve mammalian stamina.

Vazquez et al. '027 does not expressly disclose any specific compound wherein a magnesium ion is present.

Palazzi et al. '311 discloses at page 7, in claims ***2 and 5*** that the compounds "magnesium aspartate" and "potassium aspartate" may be present in compositions containing ribose. This adds a second amino acid (aspartate) to the administered composition wherein D-ribose and optionally a magnesium compound, an amino acid, and L-carnitine may be present according to **Vasquez et al. '027**.

Hayashida et al. and the relevant contents of the Asahi declaration (paragraph 3 at page 2) discloses that the administration of D-ribose to a mammal is beneficial because it is " ... well known that D-ribose has a function to promote ATP production [SIC]."

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to selected a magnesium and potassium containing salt of aspartic acid in view of the teachings of the **Palazzi et al. '311** reference because both instant cited references are directed to ribose containing compositions wherein aspartate salts. It would also have been obvious to the ordinary practitioner seeking to optimize the prior art to amend the method of **Vazquez et al. '027** by incorporating potassium and magnesium salts of aspartic acid as taught by the **Palazzi et al. '311** reference. And in view of the Asahi declaration's description of the **Hayashida** reference, one of ordinary skill would have expected that administration of D-ribose would have the instant disclosed effect because ATP production represents an energy source that is essential to cell function, and enhanced ATP production would be reasonably expected to cause enhanced cell and host performance, effectively a confirmation of the **Vasquez et al. '027** disclosures.

One having ordinary skill in the art would have been motivated to combine these references because the first two cited references are, according to their titles, directed to improving adenine nucleotide content of muscles and improving muscle performance by the administration of ribose and magnesium-ion-containing compositions to a host in need thereof, and the third reference establishes the association between D-ribose administration and

enhanced intracellular ATP production which may be interpreted to explain the effects observed in the first two references. These effects are consistent with improving the "sluggishness" in the performance of a host.

Therefore, the instant claimed methods of treatment, and ribose/carnitine/magnesium salt-containing compositions to be administered therefore, would have been obvious to one of ordinary skill in the art having the above cited references before him at the time the invention was made.

Applicant's arguments with respect to claims **1-9** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's submission of, and summary of, additional prior art.

It seems reasonable to conclude that anything done to enhance ATP production in a host, including administration of D-ribose, would be expected to generate improvements in the performance of the host so treated, including overcoming symptoms associated with depression. This view is confirmed by Chapter 2 of the Merck Manual (see PTO-892 ref. **T**) wherein the symptoms of malnutrition, including "irritability" and "apathy," are overcome by the simple step of adding the necessary nutrients to the diet of the malnourished host.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. §1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. §1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Group 1600 via facsimile transmission (FAX). The transmission of such papers must conform with the notice published

in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX (unofficially) directly to Examiner's computer is 571-273-0651. The telephone number for sending an Official FAX to the PTO is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. S. Anna Jiang, can be reached at **571-272-0627**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status Information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see < http://pair-direct.uspto.gov >. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

/L. E. C./

Patent Examiner, Art Unit 1623

LECrane:lec
06/20/2008

/Shaojia Anna Jiang, Ph.D./
Supervisory Patent Examiner, Art Unit 1623